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EXAMINER	
REDDIG, PETER J	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 09/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/685,665	VARNER, JUDITH A.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,9-12,15,19,20,55-72,75 and 80-120* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9-12,15,19,20,55-72,75 and 80-120* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/11/05, 3/11/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Election filed 07/18/06 in response to the Office Action of 05/19/06 is acknowledged and has been entered.

Applicant's election with traverse of Group I, claims 1-3, 9-12, 15, 19, 20, 55-67, 75, 80-96, 99-120 is acknowledged. The traversal to the Groups is on the grounds that claims 1-3 and 55, for example, are generic (or genus) claims that are directed to "reducing or inhibiting angiogenesis in a tissue". Applicant argues that instant claims 1-3 and 55 are all generic, or genus, claims within the definition of MPEP 806.04(d). For example, applicant argues, the claims do not limit the tissue to that associated with any "pathological condition". Applicant argues that the tissue is also not limited to "cancer" or " the eye".

Upon review and reconsideration, the claims of Groups I and II will be rejoined.

The applicant's traversal to the species election is that the instant claims recite processes, not combinations or single compounds, and so no common structural feature need be present. Instead, only a "property in common" is necessary. Applicant argues that one such "property" is present in that each of the alleged members is treated by inhibiting angiogenesis in tissue via an antibody or antibody fragment of the invention. Applicant argues that each of the nine alleged species does have a function related property such that they may not be subject to restriction.

Upon review and reconsideration, all species are rejoined.

2. Claims 1-5, 9-12, 15, 19, 20, 55-72, 75, and 80-120 are pending.

3. Claims 1-5, 9-12, 15, 19, 20, 55-72, 75, and 80-120 are currently under consideration.

Specification Objections

4. The abstract of the disclosure is objected to because it is greater than 150 words. Correction is required. See MPEP § 608.01(b).

5. The disclosure is objected to because of the following informalities:

The alpha is missing from alpha 5 beta 1 on p. 44, line 11.

The word significant on p. 52, line 28, should be significantly

Appropriate correction is required.

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Methods for inhibiting angiogenesis.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 118-120 is indefinite because it recites the phrase a "chimeric antibody". Although the specification teaches that term "antibody" encompasses a chimeric antibody the exact meaning of the word chimera is not known. The term chimera is generic to a class of antibodies which are products of genetic shuffling of antibody domains and other active proteins. The term encompasses antibodies fused to non-immunoglobulin proteins as well as antibodies wherein any domain of the antibody is substituted by corresponding regions or residues of human antibodies including but not limited to CDR grafted antibodies. Thus the metes and

bounds of the claim protection sought cannot be determined.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-5, 9-12, 15, 19, 20, and 80-88 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing or inhibiting angiogenesis in a tissue comprising contacting alpha 5 beta 1 integrin in the tissue with an agent, wherein said agent comprises an anti-alpha 5 beta 1 antibody or an alpha 5 beta 1 binding fragment of said antibody and said agent interferes with specific binding of the alpha 5 beta 1 integrin to **fibronectin** expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue , does not reasonably provide enablement for a method of reducing or inhibiting angiogenesis in a tissue , comprising contacting alpha 5 beta 1 integrin in the tissue with an agent, wherein said agent comprises an anti-alpha 5 beta 1 antibody or an alpha 5 beta 1 binding fragment of said antibody and said agent interferes with specific binding of the alpha 5 beta 1 integrin to a **ligand** expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to a method of reducing or inhibiting angiogenesis in a tissue, comprising contacting alpha 5 beta 1 integrin in the tissue with an agent, wherein said agent comprises an anti-alpha 5 beta 1 antibody or an alpha 5 beta 1 binding fragment of said antibody

and said agent interferes with specific binding of the alpha 5 beta 1 integrin to a ligand expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue.

This means that the claims are drawn to inhibiting angiogenesis by interfering with the specific binding alpha 5 beta 1 to **any** ligand in the tissue.

The specification teaches that angiogenesis is involved in such diverse diseases as cancer, ocular disease and inflammatory diseases and this has led to an effort to identify methods for specifically inhibiting angiogenesis as a means to treat these diseases, see p. 4, lines 1-5.

Furthermore, the specification teaches that the invention relates generally to methods for treating conditions involving undesirable angiogenesis and more specifically to methods of inhibiting angiogenesis by interfering with specific binding of alpha 5 beta 1 integrin to a ligand, p.1 lines 14-18.

The specification teaches that alpha 5 beta 1 is a receptor for fibronectin and that alpha 5 beta 1 is generally selective for fibronectin, p13, lines 3-15. The specification teaches that alpha 5 beta 1 function blocking antibodies block by human umbilical vein endothelial cell attachment to fibronectin and migration on fibronectin, see para bridging p.44-45 and p. 45, lines 9-18. The specification teaches that in the *in vivo* chick chorioallantoic membrane (CAM) angiogenesis assay that the ability of cells to interact with fibronectin through the alpha 5 beta 1 integrin is important for angiogenesis *in vivo,* see p.45-48. The specification teaches that intact fibronectin and a cell binding fragments of fibronectin enhanced angiogenesis in the CAM assay while a fragment of fibronectin that did not bind cells did not enhance angiogenesis, see p.46, lines 20-35. The specification also teaches that function-blocking antibodies to alpha 5 beta 1 blocked angiogenesis in the CAM angiogenesis assay, see p. 47, lines 1-15. The specification teaches

also teaches that the function blocking alpha 5 beta 1 antibodies could block stimulated angiogenesis in human skin grafted onto mice, see Example 3. Additionally, the specification teaches that the function blocking alpha 5 beta 1 antibodies could block tumor associated angiogenesis induced by human tumor cells in the CAM angiogenesis assay, see Example 4.

One cannot extrapolate the teachings of the specification to the scope of the claims as broadly claimed because alpha 5 beta 1 binds only to fibronectin and fibrinogen and neither the specification nor the art of record provide a nexus between fibrinogen and alpha 5 beta 1 mediated angiogenesis.

In particular, Ruoslahti (WO95/14714, 1995, IDS) teaches that the only known ligand for alpha 5 beta 1 is fibronectin, see p. 2 lines 3-4. Additionally, Suehiro et al. teach (Journal of Biological Chemistry, 1997, 272: 5360-5366, IDS) teach the identification of fibrinogen as a novel ligand for the integrin alpha 5 beta 1, see abstract and p. 5360, right column. Thus, the only ligands to which the integrin alpha 5 beta 1 specifically binds are fibronectin and fibrinogen. Thus, these are the only alpha 5 beta 1 ligands to which an alpha 5 beta 1 antibody can block specific binding. Thus, given the specificity of alpha 5 beta 1 for fibronectin and fibrinogen and the fact the role of fibrinogen in alpha 5 beta 1 regulation of angiogenesis is unknown, one of skill in the art could not reasonably predict without undue experimentation that interfering with specific binding of alpha 5 beta 1 to any ligand, other than fibronectin, would reduce or inhibit angiogenesis in a tissue.

Applicant is reminded that MPEP 2164.03 teaches "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 428 F.2d 833, 166 USPQ 18, 24 (CCPA

1970) the amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly state in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order for it to be enabling. Given only lack of guidance in the specification, no one skilled in the art would accept the assertion that the claimed invention would function as contemplated or as claimed based only on the information in the specification and that known in the art at the time the invention was made.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the invention will function as contemplated with a reasonable expectation of success. For the above reasons, it appear that undue experimentation would be required to practice the claimed invention.

9. Claims 55-72, 75, 89-120 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing or inhibiting angiogenesis in a tissue in an individual or a method of reducing the severity of a pathological condition associated with angiogenesis in an individual, comprising contacting alpha 5 beta 1 integrin in the tissue with an agent, wherein said agent comprises a **humanized** anti-alpha 5 beta 1 antibody or a **humanized** alpha 5 beta 1 binding fragment of said antibody and said agent interferes with

specific binding of the alpha 5 beta 1 integrin to **fibronectin** expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue , does not reasonably provide enablement for a method of reducing or inhibiting angiogenesis in a tissue or in a tissue in an individual or a method of reducing the severity of a pathological condition associated with angiogenesis in an individual, comprising contacting alpha 5 beta 1 integrin in the tissue with an agent, wherein said agent comprises an anti-alpha 5 beta 1 antibody or an alpha 5 beta 1 binding fragment of said antibody and said agent interferes with specific binding of the alpha 5 beta 1 integrin to a **ligand** expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to a method of reducing or inhibiting angiogenesis in a tissue in an individual or a method of reducing the severity of a pathological condition associated with angiogenesis in an individual, comprising contacting alpha 5 beta 1 integrin in the tissue with an agent, wherein said agent comprises an anti-alpha 5 beta 1 antibody or an alpha 5 beta 1 binding fragment of said antibody and said agent interferes with specific binding of the alpha 5 beta 1 integrin to a ligand expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue.

This means that the claims are drawn to *in vivo* anti-angiogenesis therapies in which **any** anti-alpha 5 beta 1 antibody which interferes with specific binding of the alpha 5 beta 1 integrin to **any** ligand expressed in a tissue is used for reducing or inhibiting angiogenesis in the tissue of diseases associated with increased angiogenesis.

The specification teaches that angiogenesis is involved in such diverse diseases as cancer, ocular disease and inflammatory diseases and this has led to an effort to identify methods for specifically inhibiting angiogenesis as a means to treat these diseases, see p. 4, lines 1-5. Furthermore, the specification teaches that the invention relates generally to methods for treating conditions involving undesirable angiogenesis and more specifically to methods of inhibiting angiogenesis by interfering with specific binding of alpha 5 beta 1 integrin to a ligand, p.1 lines 14-18. The specification further teaches that alpha 5 beta 1 is a receptor for fibronectin and that alpha 5 beta 1 is generally selective for fibronectin, p13, lines 3-15.

One cannot extrapolate the teachings of this specification to the scope of the claims because one cannot not use **any** antibody, such as the mouse monoclonal antibody to alpha 5 beta 1 exemplified in the specification (para. bridging p. 44 and 45), to treat patients (i.e. humans) because antibodies that have not been modified to reduce their antigenicity (i.e. humanized) will elicit an immune response. It is well known in the art that the immune response will reduce the effectiveness of the treatment and be problematic for the patient.

In particular, as drawn to this issue, Winter et al (TIPS, 1993, 14:139-143) specifically teach that a major problem with the use of murine monoclonal antibodies in the treatment of human subjects is the development of human antimouse antibodies (HAMA) that can inactivate the injected antibodies. Thus, it would be expected that the injection of cross species antibody would result in anti-other species antibodies and/or cytotoxic T cells against the injected antibody. Further, Baselga et al (J. Clin. Oncol, 1996, 14:737-744) specifically teach that murine antibodies are limited clinically because they are immunogenic.

Given the above, it is clear that it is not possible to predict that any antibody to alpha 5 beta 1 integrin that interferes with specific binding of the alpha 5 beta 1 to a ligand expressed in the tissue would successfully treat a human tumor or a pathological condition associated with the eye in a human. Thus it would require undue experimentation to practice the broadly claimed invention.

Furthermore, one cannot extrapolate the teachings of the specification to the scope of the claims as broadly claimed because alpha 5 beta 1 binds only to fibronectin and fibrinogen and neither the specification nor the art of record provide a nexus between fibrinogen and alpha 5 beta 1 mediated angiogenesis.

In particular, Ruoslahti (WO95/14714, 1995, IDS) teaches that the only known ligand for alpha 5 beta 1 is fibronectin, see p. 2 lines 3-4. Additionally, Suehiro et al. teach (Journal of Biological Chemistry, 1997, 272: 5360-5366, IDS) teach the identification of fibrinogen as a novel ligand for the integrin alpha 5 beta 1, see abstract and p. 5360, right column. Thus, the only ligands to which the integrin alpha 5 beta 1 specifically binds are fibronectin and fibrinogen. Thus, these are the only alpha 5 beta 1 ligands to which an alpha 5 beta 1 antibody can block specific binding. Thus, given the specificity of alpha 5 beta 1 for fibronectin and fibrinogen and the fact the role of fibrinogen in alpha 5 beta 1 regulation of angiogenesis is unknown, one of skill in the art could not reasonably predict without undue experimentation that interfering with specific binding of alpha 5 beta 1 to any ligand, other than fibronectin, would reduce or inhibit angiogenesis in a tissue.

Applicant is reminded that MPEP 2164.03 teaches "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the

art as well as the predictability of the art. In re Fisher, 428 F.2d 833, 166 USPQ 18, 24 (CCPA 1970) the amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly state in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order for it to be enabling. Given only lack of guidance in the specification, no one skilled in the art would accept the assertion that the claimed invention would function as contemplated or as claimed based only on the information in the specification and that known in the art at the time the invention was made.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the invention will function as contemplated with a reasonable expectation of success. For the above reasons, it appear that undue experimentation would be required to practice the claimed invention.

Double Patenting

10. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

11. Claims 55 and 56 rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 2 and 3 of prior U.S. Patent No. 6,852, 318. This is a double patenting rejection.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they relate to the same inventive concept wherein both the patented claims and the instant claims have all of the characteristics of a method of reducing or inhibiting angiogenesis in a tissue in an individual, comprising contacting alpha 5 beta 1 integrin in the tissue with an agent, wherein said agent comprises an anti-alpha 5 beta 1 integrin antibody or an alpha 5 beta 1 integrins binding fragment of said antibody, and said agent interferes with specific binding of the alpha 5 beta 1 integrin to a ligand expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue, wherein the individual is a human.

Although the patented claims specifically state that the antibody is an antagonist and the instant claims state that the antibody is an agent and the patented claims state that the agonist induces growth factor stimulated endothelial cell apoptosis and interferes with the specific binding, given that the method of the issued patent comprises the same method steps as claimed in the instant invention, that is, reducing or inhibiting angiogenesis in a tissue in an individual, comprising contacting alpha 5 beta 1 integrin in the tissue with an agent, wherein said agent comprises an anti-alpha 5 beta 1 integrin antibody or an alpha 5 beta 1 integrins binding fragment of said antibody, and said agent interferes with specific binding of the alpha 5 beta 1 integrin to a ligand expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue in the same population, and the claimed method would inherently lead to the induction of

growth factor stimulated endothelial cell apoptosis. Thus the scope of the two methods is identical and the patented claims and the instant claims are coextensive.

12. Claims 57-72 and 75 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 3 and 14-29 of US PATENT NO: 6,852, 318. This is a double patenting rejection.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they relate to the same inventive concept wherein both the patented claims and the instant claims have all of the characteristics of a method of reducing the severity of a pathological condition associated with angiogenesis in an individual, comprising contacting alpha 5 beta 1 integrin in the tissue with an agent, wherein said agent comprises an anti-alpha 5 beta 1 integrin antibody or an alpha 5 beta 1 integrins binding fragment of said antibody, and said agent interferes with specific binding of the alpha 5 beta 1 integrin to a ligand expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue and reducing the severity of the pathological condition, wherein the pathological condition is a neoplasm, wherein the neoplasm is a malignant neoplasm or metastatic malignant neoplasm and is a carcinoma or sarcoma, wherein the individual is a human, wherein the agent is administered intravenously, orally, or into a neoplasm, wherein the pathologic condition is associated with the eye, wherein the pathological conditions of the eye are selected from the group including diabetic retinopathy and macular degeneration by neovascularization, wherein the agent is administered in the form of eye drops, intravenously, or orally for the pathological condition associated with the eye, and wherein the agent is administered at a dose of 0.0001 to 100 mg/kg body weight.

Although the patented claims specifically state that the antibody is an antagonist and the instant claims state that the antibody is an agent and the patented claims state that the agonist induces growth factor stimulated endothelial cell apoptosis and interferes with the specific binding, given that the method of the issued patent comprises the same method steps as claimed in the instant invention, in the same population, that is, reducing the severity of a pathological condition associated with angiogenesis in an individual, comprising contacting alpha 5 beta 1 integrin in the tissue with an agent, wherein said agent comprises an anti-alpha 5 beta 1 integrin antibody or an alpha 5 beta 1 integrins binding fragment of said antibody, and said agent interferes with specific binding of the alpha 5 beta 1 integrin to a ligand expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue and reducing the severity of the pathological condition, wherein the pathological condition is a neoplasm, wherein the neoplasm is a malignant neoplasm or metastatic malignant neoplasm and is a carcinoma or sarcoma, wherein the individual is a human, wherein the agent is administered intravenously, orally, or into a neoplasm, wherein the pathologic condition is associated with the eye, wherein the pathological conditions of the eye are selected from the group including diabetic retinopathy and macular degeneration by neovascularization, wherein the agent is administered in the form of eye drops, intravenously, or orally for the pathological condition associated with the eye, and wherein the agent is administered at a dose of 0.0001 to 100 mg/kg body weight. Given the above, the method of the instant claims would inherently lead to the induction of growth factor stimulated endothelial cell apoptosis. Thus the scope of the two methods is identical and the patented claims and the instant claims are coextensive.

13. The non-statutory double patenting rejection, whether of the obviousness type or non-obviousness type, is based on a judicially created doctrine grounded in public policy (a policy relected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 438, 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed b the assignee must fully comply with 37 CFR 3.73(b)

14. Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 2 of US PATENT NO: 6,852, 318. Although the conflicting claims are not identical, they are not patentably distinct from each other because they relate to the same inventive concept and would have been obvious in view of the patented claims which have all of the characteristics of a method of reducing or inhibiting angiogenesis in a tissue, comprising contacting alpha 5 beta 1 integrin in the tissue with an agent, wherein said agent comprises an anti- alpha 5 beta 1 integrin antibody or an alpha 5 beta 1 integrins binding fragment of said antibody, and said agent interferes with specific binding of the alpha 5 beta 1 integrin to a ligand expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue.

Closest Prior Art

15. The closest prior art is Davis et al. (Journal of Cellular Biochemistry, 1993, 51:206-218) which teaches the inhibition of endothelial cord formation *in vitro* by human umbilical vein endothelial cells with a polyclonal antibody to the alpha 5 beta 1 integrin, see abstract and Fig. 2 and 3. They do not teach the use of the antibody in a tissue and teach that the effects of the alpha

5 beta 1 antibody does not interfere with the specific binding of alpha 5 beta 1 to its ligand, see Fig. 3 and p. 214 right column and para. bridging p. 215 and 216.

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Peter J. Reddig, Ph.D.
Examiner
Art Unit 1642

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

PJR